previously submitted election of species requirement. At the present time, Applicant elects the species comprising murine IgG1 antibodies with three modifications in the Fc hinge region (claims 1-10). Within this species, Applicants further elect initial consideration of the species of murine IgG1 antibodies with three mutations in the Fc hinge region, wherein amino acid 252 is leucine, 254 is serine, and 256 is phenylalanine.

C. Rejection of Claims 1-10 under 35 U.S.C. § 112

The Action rejected claims 1-10 under 35 U.S.C. § 112, first paragraph as lacking enabling support in the specification. The Action states that the identity of the Kabat Ig sequence incorporated into the specification by reference must be disclosed to enable the claims. The Action requests that a sequence list and identifier for the Kabat sequence be included.

Applicant would like to reiterate that claims 5 to 7 refer to amino acid positions generic to immunoglobulins. At page 6, lines 12-20, the specification teaches:

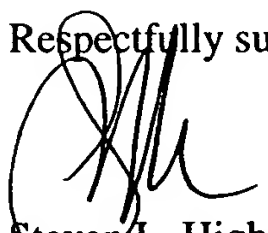
> More particularly, the present invention concerns mutant Ig domains and antibodies containing domains in which one or more of the following amino acids have been exchanged for other residues: threonine (thr) at position 252, threonine at position 254, threonine at position 256 (wherein the amino acids are numbered according to Kabat *et al.*, (1991)). To increase the half life of an Fc-hinge domain, or intact antibody, any of the above residues may be substituted for any other amino acid residue and then variants that have higher affinity for FcRn may be selected using bacteriophage display, for example, or by any other method known to those of skill in the art. Substitution can advantageously be achieved by any of the molecular biological techniques known to those of skill in the art, as exemplified herein below, or even by chemical modification.
>
> Certain increased half-life antibodies or domains will be those which include one or more of the following substitutions on the Kabat numbering system, or their equivalents on different numbering systems: threonine (thr) 252 to leucine (leu) 252, threonine 254 to serine (ser) 254 threonine 256 to phenylalanine (phe) 256. An example as disclosed herein is the triple mutant termed LSF which contains the three mutations: threonine 252 to leucine 252, threonine 254 to serine 254 threonine 256 to phenylalanine 256.

Thus, the amino acids referred to in claims 5 to 7 are not restricted to the sequence listing, but are generic positions as would be understood by one of ordinary skill in the art in light of the teachings of the specification. One of ordinary skill in the art would recognize that the Kabat sequence listing provides a standard format for the numbering of conserved regions within molecules of immunological interest. One of ordinary skill would further recognize that listing specific residues in accordance with Kabat provides the requisite teaching for analogous modifications of any immunoglobulin. The modification of the specific residues taught by the specification leads directly to an increase in the serum half-life of an immunoglobulin molecule. This modification should not be considered applicable only to the sequence set forth in the SEQ ID NO:37, but rather that this molecule provides a template upon which such modifications may be modeled for other Ig species. One of skill would recognize that the Kabat reference simply supplies a system of nomenclature that enables the application of the modifications made in one template to increase the serum half-life of other immunoglobulin molecules. Therefore, SEQ ID NO:37 has been provided solely to illustrate what positions in the Ig molecule the numbering refers to rather than to limit the scope of the invention to a single murine IgG species.

However, the specification has been amended to include the requested subject matter. Applicant submits the new sequence listing in order to expedite the prosecution of this application. Included with this response is an amended sequence listing, an additional hard copy, a computer readable form, and a declaration by the undersigned attorney for the Applicant, asserting that the amendment includes no new matter.

The Examiner is invited to contact the undersigned attorney at 512-418-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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APPENDIX A

1. A composition comprising a mutant IgG molecule having an increased serum half-life relative to IgG, and wherein said mutant IgG molecule has at least one amino acid substitution in the Fc-hinge region.

2. The composition of claim 1, wherein said IgG is a human IgG.

3. A composition comprising a mutant IgG Fc-hinge fragment having an increased serum half-life relative to the serum half-life of IgG, and wherein said fragment has an increased binding affinity for FcRn.

4. A composition comprising a mutant IgG Fc-hinge fragment having an increased serum half-life relative to the serum half-life of IgG, and wherein said fragment has the same or slightly lower affinity than IgG for binding to FcRn.

5. The composition of claim 1 or 3, wherein said molecule or fragment has an amino acid substitution at one or more of the amino acids selected from number 252, 254, 256, 309, 311, or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

6. The composition of claim 5, wherein said molecule or fragment has three amino acid substitutions at amino acid number 252, 254, 256, 309, 311, or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

7. The composition of claim 6, wherein said molecule or fragment has the following amino acid substitutions: leucine for threonine at position 252, serine for threonine at position 254 and phenylalanine for threonine at position 256.

8. The composition of claim 1 or claim 3, wherein said molecule or fragment has a dissociation constant for binding to FcRn at pH 6, of less than about 7 nM as measured by surface plasmon resonance analysis.

9. The composition of claim 1 or claim 3 further defined as a pharmaceutically acceptable composition.

10. The composition of claim 5, wherein said amino acid substitutions are generated by random mutagenesis.